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REMARKS

This paper is in response to the Office Action dated February 17, 2006, for the above-identified application. A response to the office action was originally due on May 17, 2006. Applicants are filing this response with a request for a three-month extension of time, thus making this paper timely if sent on or before the new filing date of August 17, 2006.

Claims 1-21 are pending in the application. Claims 1-3, 5, 9, 11, 13, 14, 20 and 21 are objected to. Applicants have amended claims 1, 5, 10, 12, 15 and 16. Claims 4, 6-8, 14 and 17-19 have been canceled. No new subject matter has been added to the subject application with the filing of this response. Applicants reserve their right to file divisional applications on the subject matter that has been subject to restriction and continuation applications on the subject matter that has been deleted out of all currently amended claims. Applicants respectfully point out that the amendment of claims 10, 15 and 16 and cancellation of claims 14 and 17-19 are in response to the Examiner's §112 rejections (see below).

Restriction Requirement

The Examiner stated that the applicants' election with traverse of group I is acknowledged, wherein X and Z are N and g is 0. Applicants have amended claim 1 and claim 5 to reflect the election of Group I. Further claims 4 and 6-8 have been canceled in response to the election of Group I. Applicants wish to thank the Examiner for the rejoinder of method claims 10 and 12-16.

Therefore, applicants respectfully suggest that the claims are now in condition for allowance.

35 USC §112, First Paragraph

The Examiner stated that claims 10, 12 and 15-16 are rejected under §112, first paragraph for enablement issues.

In response, applicants have amended claims 10 and 12 so that they are now directed to metabolic disorders, hyperphagia or diabetes. Applicants have added the disease diabetes to claim 12. Support for this amendment can be found throughout the specification and in claims 1 and 10. Applicants have canceled claim 14.

Applicants respectfully suggest that obesity is directly linked to obesity-induced diabetes. Applicants respectfully note that the Examiner has acknowledged the utility of NPY Y5 antagonists for hyperphagia, obesity and diabetes. Applicants respectfully suggest that not only hyperphagia, but other metabolic disorders that are regulated by the NPY Y5 receptor, can be treated with the claimed compounds of the invention. Applicants respectfully suggest that treatment of these disorders are enabled. In support of this position, applicants are providing the following web page (**http://www.scienceden.com/mblology/research/obesity**, hard copy attached). Said web page discusses the role that neuropeptide receptors play in various metabolic disorders, such as obesity as well as insulin resistance.

Applicants therefore, respectfully request the withdrawal of this objection.

35 USC §112, Second Paragraph

The Examiner stated that claims 15-16 are rejected under §112, second paragraph.

In response, applicants have amended claims 15-16 so they are directed to the treatment of disorders caused by obesity. Applicants therefore, respectfully request the withdrawal of this objection.

Applicants respectfully submit that in view of the above response, applicants have sufficiently addressed the Examiner's objections and that the application, as amended, is in condition for allowance.

If any additional fees, other than the appropriate extension of fees, are determined to be due by this paper, the Commissioner is hereby authorized to deduct such fees from **Account No. 19-0365**.

The Examiner is requested to call the undersigned attorney on any matter connected with this application.

Schering-Plough Corporation
2000 Galloping Hill Road
Patent Department
K-6-1-1990
Kenilworth, New Jersey 07033-0530
Tel. (908) 298-2161
Fax. (908) 298-5388

Respectfully submitted,

By:
Name: **William Y. Lee**
Reg. No.: **46,100**

August 16, 2006

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printer friendly versions: Low Graphics Text Only

Obesity and Weight Loss

Obesity is defined as having a Body Mass Index (BMI) of over 30 and being overweight as over 25. BMI is calculated by taking a persons weight in kilograms and dividing by their height in meters squared (kg/m^2.

The 1999 - 2000 National Health and Nutrition Examination Survey (NHANES) showed that nearly 65% of adults in US are overweight, 31% of those obese. The World Health Organization (WHO) reports that being overweight is one of the top 10 risk conditions in the world - the top 5 in developed countries. Obesity increases the risk for type II diabetes, heart attacks, stroke and some cancers.

This obesity epidemic is caused by both biological and environmental factors. The environmental factors include the overconsumption of food due to its increased availability, lower prices, high calorie density and good taste. In addition the trend towards a less active lifestyle results in the reduction of energy expenditure.

A number of molecules have been discovered to be involved in controlling weight regulation, appetite, and metabolism levels. These molecules include leptin, neuropeptide Y (NPY), agouti-related peptide (AgRP), alpha-melanocyte-stimulating hormone (alpha-MSH), cholecystokinin, ghrelin and insulin.

Leptin

Leptin was discovered in 1994 after finding its gene was mutated in an obese strain of mice. Treating these mice with leptin decreased their appetite and increased their metabolism resulting in weight loss. Decreased levels of leptin cause only a small percent of human obesity cases. In these cases of extreme obesity, treatment with leptin is successful. Most obese people already have higher than normal leptin levels however, but are resistant to its effects. The reason for this is not known but may indicate that the main role of leptin is to protect against weight loss when food is scarce.

Leptin is produced by fat cells and when the amount of stored fat decreases, leptin levels also decrease. This results in an increase in appetite and a decrease in metabolism. Higher levels of leptin do not result in a decrease in appetite

Quote of the Month

"Who are we? Where do we come from? Why are we this way and not some other? What does it mean to be human? Are we capable, if need be, of fundamental change, or do the dead hands of forgotten ancestors impel us in some direction, indiscriminately for good or ill, and beyond our control? Can we alter our character? Can we improve our societies? Can we leave our children a world better than the one that was left to us? Can we free them from the demons that torment us and haunt our civilization? In the long run, are we wise enough to know what changes to make? Can we be trusted with our own future?"

- Carl Sagan, Shadows of Forgotten Ancestors (p.4)

or an increase in metabolism however.

The arcuate nucleus (ARC) is a region of the brain within the hypothalamus. The receptors for leptin are located on the neurons in this region.

(skip Flash animation)

Leptin and Obesity

Hold your mouse over the buttons below to see what happens with:

- a stable body weight,

- when you eat less, exercise more

- eat more exercise less

- or with obesity

Neuropeptide Y (NPY), Agouti-related peptide (AgRP) and alpha-melanocyte-stimulating hormone (alpha-MSH)

The arcuate nucleus (ARC) has two major types of neurons. One type makes the peptides Neuropeptide Y (NPY) and Agouti-related peptide (AgRP). These molecules increase appetite and decrease metabolism. The other type of neurons, called POMC/CART neurons, produce alpha-melanocyte-stimulating hormone (alpha-MSH), which inhibit eating.

The neurons that produce neuropeptide Y and Agouti-related peptide are activated when the amount of stored fat and leptin decreases. The POMC/CART neurons are then inhibited. This tends to lead to weight gain.

When the amount of stored fat and leptin is higher the neuropeptide Y and Agouti-related peptide producing neurons are inhibited and the POMC/CART neurons are activated, leading to weight loss.

Signals from both types of neurons are sent to other parts of the brain and eventually to the nucleus tractus solitarius, in the brain stem region of the brain.

Insulin

Insulin has receptors throughout the body including in the arcuate nucleus. Some evidence suggests that the presence of insulin in the arcuate nucleus results in an inhibition of Neuropeptide Y and a decrease in appetite.

Cholecystokinin, Ghrelin and PYY

Cholecystokinin has been known for time as being involved in regulating appetite.

Ghrelin is produced by the stomach and results in the release of growth hormone by the pituitary gland - it also causes a major increase in appetite by stimulating both Neuropeptide Y and Agouti-related peptide. Prader-Willi syndrome causes people to be really obese, and they have very high ghrelin levels, although this may be indirect. Most obese people do not have high ghrelin levels though. People who lose weight from dieting do have higher levels of ghrelin, making it much more difficult to keep the weight off.

PYY inhibits Neuropeptide Y and Agouti-related peptide, leading to a lower appetite.

Medications for Obesity and Weight Loss

Eating healthy foods and getting proper exercise are the best methods for losing weight, although many medications are also available.

Phentermine hydrochloride - believed to suppress appetite centers in the brain. Brand names of phentermine include Ionamin and Adipex-P.

Meridia - generic name is sibutramine hydrochloride monohydrate, it is an amphetamine like drug that inhibits the activity of norepinephrine and serotonin

Xenical - works by preventing the digestion and absorption of fat by blocking lipases. Lipases are enzymes that digest fat.

Related Web Sites

Obesity at Diseases Explained - information about obesity and including Patient Booklets and posters for purchasing.

DrDonnica.com - DrDonnica.com is a user-friendly women's health information site dedicated to women by a leading women's health expert and advocate, this link goes directly to her Weight Loss Health Center section.

Aphrodite - the latest news on important women's health issues, such as diet & weight loss, menopause, hormone replacement therapy, anti-ageing, infertility, wellbeing and female sexuality.

TOAST (The Obesity Awareness & Solutions Trust) - first UK charity to set up actions groups, to inform, educate and listen, to research and to work with interested parties to raise the profile of a set of problems called obesity. TOAST seeks to promote good contacts in industry, academic and patient groups and provide an effective means of dialogue with policy makers and regulators.

The Donald B. Brown Research Chair - The Donald B. Brown Research Chair on Obesity is devoted to the understanding of obesity through research projects, to training and continuing education on obesity to graduate students and health professionals, and to inform the medias and the public about obesity issues in our society.

References

Cellular Warriors at the Battle of the Bulge
Science Vol. 299 February 7, 2003 p. 846
Jean Marx

Obesity Drug Pipeline Not So Fat
Science Vol. 299 February 7, 2003 p. 849
Trisha Gura

A Sympathetic Defense Against Obesity
Science Vol. 297 August 2, 2002 p. 780
Abdul G. Dulloo

Article originally written by All ScienceDen.com on: Feb 27, 2003

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